Notice of Allowability	Application No.	Applicant(s)	
	09/744,866	AUSTRUP ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *31 October 2006 by the B.P.A.I.*

2. ☒ The allowed claim(s) is/are *24 and 28*.

3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☒ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____.
7. ☐ Examiner's Amendment/Comment
8. ☒ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

S. Rawlings
Art Unit 1643

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

The claims are directed to a method for isolating tumor cells, said method comprising passing a fluid containing tumor cells through a screen having pores of about 15 to 30 micrometers (μm) in width, such that the tumor cells are retained on the screen.

The size of a cell is about 10 μm in diameter, though some cells are larger and others are smaller. Nishiya et al. (*Acta Med. Okayama.* 1976 Apr; **30** (2): 143-145), for example, teaches the diameter of myeloma cells ranged from 8 μm to 12 μm; see entire document (e.g., the abstract).

Based upon the teachings of the prior art, as explained in more detail in the following paragraphs, it would be expected that cells having diameters ranging from 8 μm to 12 μm would not be retained by screens having pores of a diameter in the range of 15 to 30 μm.

For example, Sato et al. (*GANN Monograph on Cancer Research.* 1977; **20**: 3-13) teaches hepatoma and sarcoma cells are capable of passing through a membrane filter having pores of a diameter of 7.3 μm; see entire document (e.g., the abstract; page 4, Figure 1; page 6, Figure 3; and page 7, Table II.

Consistently, Khato et al. (*Tohoku J. Exp. Med.* 1979 Jul; **128** (3): 273-284) teaches sarcoma cells and leukemic cells, which were smaller than sarcoma cells, were capable of passing through filters having varying pore diameters of 5.4, 7.9, or 9.3 μm; see entire document (e.g., the abstract).

In contrast to the ability of certain hepatoma, sarcoma, and leukemia cells to pass through filters having pore diameters ranging from 5.4 μm to about 7.9 μm, as demonstrated by Sato et al. and Khato et al., the prior art teaches other cells are retained by certain filters having pore sizes of 8 μm but not by other types of filters, despite having relatively larger pore sizes.

For example, Rosenthal et al. (*Anal. Quant. Cytol.* 1979 Jul-Aug; **1** (2): 84-88) teaches the separation of epithelial cells from neutrophils is best achieved by passing a suspension containing the cells through a nylon mesh filter having pores of a diameter of 10 μm, because the epithelial cells are retained, whereas the neutrophils are not, but that the epithelial cells are too large to pass through a Nucleopore filter having pores of a diameter of 10 μm; see entire document (e.g., the abstract; page 85, Figure 1; page 85, column 2; and page 86, column 2). Thus, Rosenthal et al. teaches the material of which the filter is made, not just the size of the pores, determines whether or not cells pass through the filter or are retained on the filter.

This dependence upon the material of which the filter is composed is further illustrated by the teachings of Barrett et al. (*Acta Cytol.* 1976 Mar-Apr; **20** (2): 174-180). Barrett et al. teaches variable retention of cells contained in body cavity fluids by different types of filters having the same sized pores (i.e., 5 μm); see entire document (e.g., page 175, column 1; page 177, Table I).

The prior art thus teaches that, provided the size of the pores is small enough to retain the tumor cell, but large enough not to retain other non-tumor cells (e.g., leukocytes), filtration may be used to separate the tumor cells contained in a bodily fluid, such as blood, from non-tumor cells contained in the same bodily fluid.

The use of this principle is demonstrated, for example, by Vona et al. (*Am. J. Pathol.* 2000 Jan; **156** (1): 57-63). Vona et al. teaches that tumor cells of varying sizes may be isolated by filtration of samples comprising the cells through a polycarbonate membrane having cylindrical pores of a 8 μm diameter; see entire document (e.g., the abstract; page 58, column 2). Vona et al. suggests the disclosed filtration process may be used to separate such tumor cells from peripheral blood lymphocytes; see, e.g., page 60, Figure 1; and page 61, column 2.

After further practice of this principle, Zabaglo et al. (*Cytometry A.* 2003 Oct; **55** (2): 102-108) teaches efficient separation of breast cancer cells from leukocytes by retention of the breast cancer cells on a filter is achieved, provided the pore size is not too large; see entire document (e.g., the abstract; page 105, Figure 2). Zabaglo et al.

demonstrates that once the size of the pore is increased to 14 μm in diameter, recovery of the tumor cells falls from about 100% to between 18 and 38% (page 105, Figure 2).

It is therefore submitted that were the size of a filter's pores to be steadily increased within the range of about 15 to 30 μm, fewer and fewer tumor cells would be expected to be retained on the filter as the size of its pores increased. Moreover, if a filter were to have pores of a diameter of, for example, 30 μm it is fully expected that tumor cells of a significantly smaller diameter would pass through the filter's pores and would not be retained by the filter.

Contrary to any such expectations based upon the teachings of the prior art, however, the specification exemplifies the use of the claimed invention by disclosing a process that comprises passing a fraction of a bodily fluid through a 20 μm mesh screen woven from PE threads; see Example 1 at page 35. The, at page 40, lines 21-25, the specification discloses that it was shown that it was possible to isolate tumor cells from peripheral blood using this method.

The Examiner finds no factual evidence conclusively indicating the invention, as claimed, is inoperable. See *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971) ("[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.")

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to S. Rawlings whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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slr
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